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[Page 2 of 2] Number _____ of___ 2 ___

Docket No. 14986

SPECIFICATION FOR PROVISIONAL APPLICATION FOR PATENT ENTITLED

Microfluidic Connector

Inventors

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CROSS-REFERENCE TO RELATED APPLICATIONS

This application is related to (1) Application Serial No. 10/410,313 filed April 7, 2003 (Docket No. 14135), (2) the PCT application filed contemporaneously with this application by Eksigent Technologies LLC claiming priority from Serial No. 10/410,313 and entitled Microfluidic Detection Device (Docket No. 14135-1PCT), and (3) the application filed contemporaneously with this application by Don W. Arnold and entitled Improved Detection Device (Docket No. 15034). The disclosure of each of those applications is incorporated herein by reference.

BACKGROUND OF THE INVENTION

10 Field of the Invention

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This invention relates to microfluidic connectors.

Background of the Invention

One of the major hindrances to the use of microfluidic devices, for example in conjunction with liquid chromatography columns, has been the connection between the microfluidic device and conventional components, e.g. capillary tubes, optical fibers and electrical leads.

SUMMARY OF INVENTION

This invention provides novel interconnect devices for connecting elongate components (e.g. capillaries, optical fibers or electrical leads) to microfluidic devices; novel components for use in such devices; methods for making such devices and components; methods for connecting elongate components to microfluidic devices; and novel components for use in such methods.

In preferred embodiments, the novel device and the method for using it make use of six elements: an alignment chip element (jig); carrying elements (capillaries for liquid, fibers for light, leads for electrical, etc); a sealing gasket element (and an optional reinforcing gasket retainer); a microfluidic chip element; and an aligning element that provides alignment of the alignment and microfluidic chip elements during assembly and disassembly; and a holding element that holds the alignment and microfluidic chips in place once the connection is made. Each of these elements can be novel and inventive in its own right, and thus form part of the invention.

The alignment jig and microfluidic chips are preferably microfabricated with matching dimensions to promote the alignment. The microfabrication preferably produces channels in planar substrates with geometries that match that of the carrying element so that carrying elements can be readily inserted with minimal dead volume. The carrying element is preferably secured within the alignment chip with a uniform length of carrying element which protrudes from the alignment jig chip and inserts into the microfluidic chip. The sealing gasket (and optional retainer) can be a preformed member which is mounted onto the portion of the carrying element that protrudes from the alignment jig chip. The alignment jig chip can be mounted in the holder which provides two well-defined planes for alignment with the microfluidic chip. To connect the iig and the microfluidic chip, the microfluidic chip can be placed with the appropriate planes aligned, pushed onto the protruding carrying elements and clamped in place. The system can be designed to permit high pressure operation, for example using pressures greater than 3000 or greater than 5000 psi, for example as high as 7200 psi.. The method makes it possible for a plurality of carrying elements to be connected or disconnected in a single operation. In some embodiments, microfabricated filters and/or weirs can be integrated into the connector, for example without introduction of unnecessary volume. Optional alignment guides can be included for sensitive fiber optical assemblies to protect the face of the fiber optic in use. Optional contoured microchannel entrances to the microfluidic chip can be included to simplify assembly. Optional alignment features can be included to assist iig-to-chip alignment with the use of a jig. The feature is preferably an etched channel that, once the jig chip or microfluidic chip is diced from the wafer, produces a groove in the side of the chip that can be mated to a complementary feature on the alignment/holding elements.

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DETAILED DESCRIPTION OF THE INVENTION

In the Summary of the Invention above, the Detailed Description of the Invention, below, and the accompanying drawings, reference is made to particular features of the invention. It is to be understood that the disclosure of the invention in this specification includes all appropriate combinations of such particular features. For example, where a particular feature is disclosed in the context of a particular embodiment, a particular statement, or a particular Figure, that feature can also be used, to the extent

appropriate, in the context of other particular embodiments, Statements and Figures, and in the invention generally.

Reference will now be made to the drawings, which are schematic and not to scale, and which illustrate preferred embodiments of the invention.

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In one simple embodiment, the microconnector has an alignment jig chip, 12, carrying elements, 11, a sealing gasket, 13, an optional reinforcing gasket retainer, 15, microfluidic chips, 14, a holder, 16, that provides alignment during assembly and disassembly and a means, 17, for clamping the jig chip and alignment chip.

Preferably, the alignment jig, 12, and microfluidic chip, 14, are both microfabricated. A feature of these two components is that they have features that match at the edges where the interconnection is to be made. Particularly, the channel openings, 18, in the edge of the microfluidic chips are designed so that when the edges of the chips are aligned, the openings are aligned. In some embodiments, the dimensions (height, width and length) are designed to be the same to assist accurate alignment with simple assembly procedures. In other embodiments, the use of edges is replaced with other alignment mechanisms that do not require such precise geometric dimensions.

A preferred method of manufacture for the alignment and microfluidic chips is described below. The method preferably produces cylindrical channels in planar substrates, into which cylindrical carrying elements (the standard geometry) can be readily inserted. Channels having other cross sections, e.g. rectangular, triangular and diamond-shaped cross sections can alternatively be used. By way of example, the diameter of the carrying elements can be from $\sim 100~\mathrm{Im}$ (i.e. micrometer) in diameter to $\sim 400~\mathrm{Im}$ in diameter; the total thickness of the alignment jig and microfluidic chip can be from $\sim 1~\mathrm{mm}$ to $\sim 2~\mathrm{mm}$ thick with the microchannels centered in the elements; and the optional gasket retainers can be from $\sim 50~\mathrm{Im}$ to $\sim 250~\mathrm{Im}$ thick.

For assembly of the connector jig assembly, the carrying elements, 11, are semipermanently assembled into alignment jig chip, 12, as follows. The carrying element, 11, is inserted through the microchannel, 19, of the jig such that a small length of the element protrudes from the alignment jig chip. This protrusion length can match the thickness of the uncompressed sealing gasket, 13, or be slightly longer such that it protrudes into the microfluidic chip after assembly. Once the carrying element is positioned (preferably with a mechanical alignment guide for reproducibility from part to part), the element is fixed into place (with an adhesive, clamp, etc.) The material used for this fixing step will not be subjected to the fluids, etc. – therefore, compatibility is not of concern in its selection.

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The sealing gasket, 13, is mounted onto the portion of the carrying element. 11. that protrudes from the alignment jig chip, 12. The sealing gasket can be made from a number of materials. Optimum properties for this material are application-dependent. In certain applications, the material would preferably have excellent chemical compatibility. For high pressure operation high tensile strength is preferred. For good sealing and reversibility, some elastic properties are desirable to allow for reversible deformation of the material. In these situations the preferable materials are high-durometer elastomers made from perfluorocarbons, fluorocarbons, silicones, fluorosilicones, etc. One can also make the gaskets from non-elastomeric materials such as fluorocarbons (such as Teflon), PFA, PEEK, polyacetyl (e.g., Delrin), polypropylene, polyethylene, etc. These materials will deform less reversibly and will need to be replaced periodically. However, this is acceptable in many applications. The advantage is that these materials can be used to achieve higher operating pressures. The gasket can manufactured in a number of ways - injection molding, compression molding, punching, laser machining, conventional machining, micromachining, molding or painting in place (as with curing or RTV silicone) or photopolymerization of a precursor material.

If desired, the optional gasket retainer, 15, is mounted around the gasket, 13, either before during or after the formation and positioning of the gasket. This retainer, 15, provides mechanical support for the gasket, 13, during compression and operation at higher pressures, preventing irreversible deformation of the gasket by the pressure at the connection. The retainer can be manufactured from metals, plastics, ceramics, etc. such that the gasket is captured and supported. The decision to use the retainer is determined by the operating pressure and the selection of gasket material. The manufacture of the gasket retainer can be accomplished by a number of means known in the arts for forming small dimension metals, plastics, and/or ceramics - machining,

chemical etching, micromachining, punching, laser machining, water jet machining, bead blasting, injection molding, compression molding, etc. Alternatively, one can manufacture a composite gasket/retainer by compression forming two materials simultaneously using commercially available methods.

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Because the act of making a connection with this connector requires a very precise alignment of the edges, an alignment fixture, 16, is preferred for ease of use. The alignment jig assembly (with fixed carrying elements, gasket and optional retainer) is mounted in the holder, 16. The alignment jig assembly, 20, is positioned in the alignment fixture such that two planes of the assembly are well defined according to the design of the alignment fixture. These two planes are used for alignment of the jig with the microfluidic chip, which is similarly aligned with the alignment fixture. There are several means of defining the two planes.

To connect to the microfluidic chip, 14, the microfluidic chip, 14, is placed with the appropriate planes aligned to the alignment fixture, pushed onto the protruding carrying elements, 11, and clamped in place, 17.

Figures 2 through 4 show the assembled connector in plan and sectional views.

As shown in Figure 3, for example, instead of a single carrying element, one can use multiple carrying elements that are (dis)connected in parallel by including the appropriate ports in the microfluidic chip and the mating ports in the alignment jig chip.

For use in high-pressure connections, a gasket retainer, 13, is preferably used. The gasket surrounds and provides support for the sealing gasket under pressure-load conditions, preventing excessive distortion, or destruction, e.g. of the typical elastomeric gasket material. For lower pressure applications, a gasket retainer may be unnecessary.

To ease the installation of the carrying elements into the chips, one can contour the shape of the channel at the entrance to the microfluidic manifold. Figure 4 shows how, for example, one can taper, 21, the channel to a larger size at the opening to allow easier insertion of the capillary into the chip. Once the insertion of the carrying element is initiated into the larger opening of the contoured region, the completion of the assembly is facilitated.

As shown in Figure 5, if the carrying element, 11, is a microfluidic capillary, one can add a microfabricated weir, 30, to microfluidic chip, 14, near the output of the carrying element connector to prevent the introduction of undesired particulate material into the microfluidic chip.

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As shown in Figures 6a - 6d, for fiber optic connections, one can add additional alignment elements, 35, to the alignment jig chip, 12, that serve as fine alignment elements, protecting the face of the fiber optic during installation. Figures 6a and 6b illustrate a fiber- to-microchannel connection (as for example in Serial number 10/410313 referred to above. Figures) 6c and 6 illustrate an optic-to-optic connection. In this example, the second fiber optic, 36, is pre-positioned in a microchannel in the microfluidic chip, 14.

To make multi-carrying element connectors more robust and easier to handle, ribbonized carrying elements, 40, can be used instead of individual carrying elements. One can either separate the capillaries prior to insertion into the alignment jig, as shown in Figure 7, or design the jig such that the entire ribbon is accommodated.

One can make individual gaskets for the connectors, or a strip gasket with appropriate apertures that is cut into appropriately sized pieces for use in the connector. Shapes can be adjusted to match the application and the retaining gasket can be adjusted similarly. Figure 8 illustrates two examples of designs in which gaskets, 13, can be pre-cut and used with the optional gasket retainer, 15 for use with multi- carrying element connectors. In this case, the carrying elements are not shown.

With alternative manufacturing processes, combination gasket/retainer/carrying element assemblies, 70 and 71 in Figures 9a and 9b, can be assembled prior to assembly with the alignment jig. In Figure 9a, the retainer, 15, has a feature that is formed to receive the gasket, 13, which can be preformed or formed in place by aforementioned methods. In figure 9b, the retainer, 15, has features formed on both sides that will serve to capture a gasket, 13, which is formed in place with the carrying element, 11, in position. Note that this retainer assembly design, 71 can also be used if the carrying element, 11, is inserted into the alignment jig, 12, prior to gasket placement. However, this design is particularly amenable to making a gasket/retainer/carrying element assembly, 71, that will not be susceptible to

disassembly with normal handling. For manufacture of this design, methods for gasket formation are preferred that will allow the flow of a precursor material into the retainer, 15, and around the carrying element, 11, prior to hardening to its final state (examples are injection molding, vulcanization, etc.). A mold can be designed for this purpose, as is well known in the art. Figures 10a and 10b illustrates the assembly process for the preformed gasket/retainer/carrying element assemblies, 71, with alignment jigs, 12.

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As an alternative means for clamping the alignment jig, 11, and microfluidic chip, 14, one can use 'stand-alone' clamping mechanisms, 50. As shown in Figure 12, the clamping mechanism can fit around the entire alignment-jig/microfluidic chip assembly, 45. Alternatively, as shown in Figure 12, receiving features, 52, (such as grooves) can be formed in the top of the chip such that the clamp, 50 will fit into the receiving features, securing the two chips together, once the gasket has been compressed an appropriate amount. This approach allows for a more compact holder and clamping mechanism for the alignment jig and microfluidic chip. While a very high accuracy is desirable for the position and dimension of the receiving features, they can be defined in the top/bottom of the chip by any of a number of means such as lithography/chemical etching, laser machining, scoring with a diamond blade (i.e., dicing saw), etc. to achieve the necessary accuracy. Alignment is accomplished by careful definition of two edges of the clicking component.

One can alternatively make the alignment jig, 12, through other fabrication methods such as embossing into a plastic using microfabricated embossing molds.

Alternative methods of fabrication produce channels that are not cylindrical.

These can be used effectively with carrying elements that have matching geometries. If the matching geometries are not available, the mismatch can be accommodated through the use of adhesive filler, for example.

Figures 13 and 14 illustrate a device and method for positioning and aligning two chips utilizing features that are microfabricated into the alignment jig, 12, and microfluidic chip, 14. A side groove, 81, can be etched along each of the two side surfaces, 82, on the alignment jig, 12, and microfluidic chip, 14. A flange, 83, is added to the holder, 16. The flange has a thickness thinner than the side groove, 81, so as to fit inside the grooves of the alignment jig, 12, and the microfluidic chip, 14. Since the

side grooves are microfabricated simultaneously the microfluidic opening ports, 18, the grooves and the ports are in the same plane (as illustrated in Section A-A, Fig. 14b). The tight precision in feature geometry and spacing makes the side grooves ideal for positioning and aligning the microfluidic chip, 14, and the alignment jig, 12.

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The positioning flange, 83, must be carefully designed and fabricated, though the precision and tolerance may not be as stringent as in microfabrication processes. To make gliding and positioning work, the flange, 83, comprises at least two straight edges. one on each opposite side, their chip-touching edges carefully spaced to accommodate the spacing between the chip side grooves, 81. The flange/holder assembly can be fabricated by any of a number of methods. For example a one-piece flange/holder can be fabricated by conventional machining using a T-slot cutter to make a pocket. Alternatively, the flange/holder assembly can be made as a single-piece with the correct spacing between the two chip-touching edges and attached to the holder; or the flange can be made as two separate shim pieces that can be mounted on the chip holder and edge spacing adjusted during assembly. While machining the chip holder, 16, with flange, 83, in place can reduce the number of parts used, conventional machining is not the best method to create thin features, and this approach also offers little or no flexibility when chips with different groove spacing are used. Making flanges using two separate shim pieces provides maximum flexibility in terms of adjusting groove spacing. but holding the set spacing on the chip holder for prolonged use is not easy and readjustment/alignment of the two shim pieces is often needed. The preferred method is the fabrication of a single-piece flange that provides both the ease in fabrication and flexibility for different configurations.

In this case, the flange can be fabricated from any materials available in the appropriate thickness and of sufficient rigidity as to provide accurate alignment of the alignment jig and microfluidic chip. Since the side grooves on the chips are often fabricated with a height (i.e. the vertical spacing in Section A-A, Figure 14) between 120um (~0.0047") and 300um (~0.012"), the thickness of the positioning flange has to be smaller. A thin flange may be subject to mistakenly bending and buckling when chips glide inappropriately on the flanges. To prevent bending and buckling of the flange, it is essential to design a short flange, i.e. small chip's groove depth (i.e. the

horizontal spacing in Section A-A, Fig. 14b). It also helps if (1) the flange material is strong (such as alloy metals), and (2) when a shim piece(s) is used as a flange, a top cover is used to press down the flange to prevent it from bending and buckling upward.

The flange, 83, can be fabricated by any of a number of means that are appropriate for forming thin materials. Preferred methods include: conventional machining, laser machining, and chemical etching. Photochemical etching is the most preferred method because it offers higher precision/tolerance and does not suffer from potential mechanical/thermal stresses induced at the cutting edges (typically associated with the conventional machining and laser machining). In typical photochemical etching, patterns are lithographically defined using photoresist on a sheet metal panel that has a size of 12 in x 12 in or larger. The tolerance can be held up to +/- 0.0005in (or 13um) or better. Tight tolerance, such as one provided by the photochemical etching process, is critical for the positioning shim design.

Using a single-piece positioning shim. Figures 15a and 15b depict simple and effective designs for the positioning shim. Figure 15a is a "C"-shaped shim with two parallel corner relieves, 90, at the chip entry area. Figure 15b is another "C"-shaped shim with one corner relief 91 that is set inward with respect to the other corner. The design in Figure 15b can make the chip entry easier by aligning one chip groove 81 on one side of the flange, 82, before inserting the other groove on another side.

In order to slide chips on the positioning shim smoothly, one needs to provide enough clearance between the flange edges, 82, and the chip grooves, 81. However, too much clearance may make the chip wiggle in the positioning shims. To prevent the wiggling, a spring feature, 93, can be put on one flange to provide a force perpendicular to the gliding direction to push the chip on a chip groove. Figure 16 depicts an example this device. While other spring designs are possible, a simple cantilever can make an effective spring for the application. In the inset of Figure 16, slanted cantilevers, 94, are used as springs to push on a chip groove. The spring should provide minimal force yet enough mechanical stability once the chip slides into the proper position; therefore an interference fit (on the order of ~13um, or 0.0005") should be made between the chip groove, 81, and the spring, 93. The clearance, 95, between the spring, or more

correctly the chip groove, and the rest of the flange may be needed to make the initial chip-gliding easy.

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To further the ease of assembly, a caddy-docking station can be used. Figure 17 illustrates a possible caddy-docking station configuration, where utilizing the side grooves on the chip, a docking-positioning shim 96 attaches to an alignment jig, 12, possibly permanently, as a single docking-positioning unit 98; and a caddy-positioning shim 97 attaches to a microfluidic processing chip 14, preferably permanently, as a single caddy positioning unit 99. The single caddy-positioning unit 99 can be designed to be larger than the chip so that it provides ease to handle the unit. As long as outer edges of the positioning shims 96 and 97 can accommodate to one another, the caddy-positioning unit 99 can slide into the docking-positioning unit 98. Spring-like features described in Figure 16 can be used also to provide a force perpendicular to the gliding direction to push the caddy-positioning unit 99 onto the docking-positioning unit 97. Method of Manufacture

A pair of wafers are cleaned unless already clean. Standard wafer sizes can be used, 0.5 –1 mm thickness, 100 mm diameter, as well as any desired size. The wafer can be made of silicon, glass, silica, quartz, or other ceramic materials. Further, when using silica, glass or quartz wafers, a first surface of the pair of wafers is coated with a first layer of silicon. The layer can have a thickness of 1000-3000 Angstroms, for example. The layer can be applied via low-pressure chemical vapor (LPCVD) deposition as is well known in the art. Amorphous silicon films are preferred related to other choices like photoresist, chrome, chrome/gold or titanium/platinum combinations for their reliability in defining channels in a fused silica substrate without edge defects that result from etchant-induced adhesion failure or pinholes in the film.

A first pattern for micro-conduits is transferred into the first layer of silicon on both silica wafers. The pattern can be transferred using standard lithography methods, like the one described in the following paragraph.

A lithography mask can be generated from a drawing of the desired microconduit pattern, typically by a commercial vendor using a chrome film (~1000 Angstrom thick) on a glass substrate. If one mask is used, the same mask can be used for both wafers in the pair. Preferably, a single mask can be used that contains a mirror plane of symmetry for those micro-conduits that that are desired to be approximately circular in cross-section. The micro-conduit pattern preferably is designed such that mirror-image alignment of the pattern on each wafer will contain micro-conduit traces that substantially overlap in regions of the fluidic manifold where cylindrical channels are desired. If two masks are used, one is used for each wafer in the pair. A thin film, 1-7 micrometers, for example, of photoresist (photosensitive polymer) is placed over the layer of amorphous silicon on the pair of silica wafers. The side of each silica wafer having the thin film of photoresist is placed proximal to or in contact with the mask. The desired microconduit pattern is transferred from the masks to the layers of photoresist by exposing the photoresist to UV light through the mask followed by appropriate development and curing of the photoresist. The microconduit pattern can be transferred from the photoresist to the silicon laver on each wafer by etching the exposed amorphous silicon with wet chemical etching, using a mixture of hydrofluoric, nitric, and acetic acid, for example, or dry chemical etching, using reactive ion etching with a lowpressure (~15-mTorr) plasma of a mixture of gases that includes SF6, C2 C1F5 and Ar, for example, or any other method known in the art.

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After the first microconduit pattern is transferred into the first layer of silicon on both wafers, the first microconduit pattern is transferred into the first surface of the silica wafers so that each silica wafer has a patterned surface of conduits having a substantially semi-circular cross-section. This can be accomplished by wet chemical etching of the exposed regions of the silica. The wet chemical etching can be accomplished by timed submersion in a 49% solution of HF. Etch rates are typically on the order of 1.3 micrometers per minute for silica. As this etching process is isotropic, the microconduits that are formed in the wafers have a substantially semi-circular cross-section.

The photoresist can be removed using a mixture of sulfuric acid and hydrogen peroxide, for example. The first layer of silicon can be removed by dry or wet chemical etching, as described above.

Depending on the exact design, multiple etches can be used in the fabrication of the microfluidic detection device. For example, a first etch can be a shallow etch of about 1.5 microns and a second etch can be a deep etch of about 56 microns. Thus, the process is repeated using a second mask.

The shallow etch can be used to define the alignment marks on the wafers and any shallow structures that are to be incorporated into the design. The alignment marks are preferably shallow etched to provide improved alignment accuracy. In addition, the shallow etches can be used to provide regions of slightly larger diameter, i.e. 3 microns, when the regions that are shallow etched are subsequently deep etched.

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The deep-etched regions are preferably etched approximately ½ the diameter of the capillaries and optical fibers to be inserted plus about 1-2 micrometers to allow a minimal space for adhesive between the capillaries and optical fibers and the walls of the microconduit. For example, semicircular conduits having a radius of 56 micrometers are etched to make conduits having a circular cross-section with a 112 micrometer radius to accommodate capillaries and optical fibers having an outside diameter of 109 micrometers.

Preferably, the wafers are thoroughly cleaned with acid and base cleaning solutions so that surfaces of the pair of wafers are hydrophilic. In addition, the wafers preferably are also megasonically cleaned so that the surfaces of the wafers are more hydrophilic.

The first surfaces of each wafer are secured together so that the patterns on the first surfaces form the flow path 14. The cleaned, patterned surfaces of the pair of silica wafers are substantially aligned and brought into contact so that the patterned surfaces form conduits having a substantially circular cross-section. The conduits can form the flow path 14 and a place to insert the arms 28 and 32 and, optionally other microfluidic components. Preferably, the alignment is accurate to within 3 micrometers. The patterned surfaces can be aligned using a commercially available wafer alignment device, such as the Electronic Visions EV520 aligner, which allows visual alignment of the two wafers while they are maintained co-planar with a very small separation by placing removable thin (40 microns) spacers between the wafers and avoiding contact of the two wafers prior to complete alignment through the adjustment of high precision positioning stages. With the alignment complete, the wafers are clamped with the spacers remaining between the wafers. A modest pressure (approximately 2-20 psi) is

applied at the center of the wafers, normal to the plane of the wafers. At this point, a weak attachment between the wafers occurs as indicated by the visually observable bonding front that moves from the center to the edge of the wafer. As the bonding front forms, the spacers are removed so that the entire wafer finishes bonding.

The pair of wafers is heated so that they bond together permanently. Heating the wafers (to approximately 1165°C for silica wafers) for about 4-8 hours is sufficient to drive a dehydration reaction at the interface of the two wafers resulting in an interfacial bonding of the two wafers. The exact bonding temperature is dependant on the materials of construction of the wafer. The result is a strong wafer bond in which the interface essentially disappears and the resultant part is a solid component in which microconduits of substantially circular cross section exist for the introduction of fluid, capillaries, optical fibers, electrical leads, etc.

After bonding, the conduits can be filled with wax or some other suitable sacrificial material to avoid particulate contamination of the microconduits when the wafers are diced into multiple microfluidic devices 10. A diamond saw can be used to dice the wafers. Removal of the wax can be accomplished by pyrolysis of the wax. 650° is a sufficient temperature for pyrolysis. Since the microfluidic devices can be very small, dicing a single pair of bonded silica wafers can yield a large number of microfluidic detection devices 10 and hence, the cost of manufacture of the devices can be lessened.

What is claimed is:

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A microconnection substantially as illustrated in Figure 1.















